The opinion in support of the decision being entered today was not written for publication and is not precedent of the Board

Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte ANDREW S. JANOFF,
JOYCE RAUCH and THEODORE F. TARASCHI

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Appeal No. 1999-0161
Application 08/441,567

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ON BRIEF

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Before Spiegel, Scheiner, and Mills, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

This is a decision on appeal under 35 U.S.C. ' 134 from the examiner's final rejection of claims 14-20 and 50-70 are the only claims pending in this application and the subject of this appeal.

We reverse.

Claims 14, 50 and 61 are illustrative of the claims on appeal and read as follow:

14. A method for determining the presence of lupus anticoagulants in a patient's plasma which comprises the steps of:

(a) obtaining first and second samples of the patient's plasma;

(b) combining a detergent and a phospholipid so as to obtain an aqueous suspension comprising the particles[1] containing the detergent and the phospholipid;

(c) incubating the first sample with the aqueous suspension;

(d) performing a lipid-dependent diagnostic assay on both the first and second samples, the assay producing a positive reading when used on a sample which contains lupus anticoagulants; and

(e) comparing the results of the assays performed on the first and second samples, the presence of a normal result for the first sample and a positive result for the second sample being indicative of the patient having lupus anticoagulants;

wherein the phospholipid has a hexagonal (H_{II}) phase organization in aqueous detergent-free media, wherein the detergent is a lupus assay-compatible detergent, wherein the particles comprising the phospholipid and detergent have diameters of less than about 50nm, wherein the phospholipid remains in suspension at a temperature of 25ÅC for at least one hour, and wherein the detergent, in combination with the phospholipid, is capable of inhibiting lupus anticoagulant, and not interfering with the anticoagulant effect of heparin, anti-Factor antibodies and factor deficiencies.

[1] See specification page 5, paragraph 2, and Brief, page 2, paragraph 2.

50. A method of reducing false positive results from a lipid-dependent diagnostic assay performed on a blood sample obtained from a patient having an autoimmune disorder characterized by the presence of anti-phospholipid antibodies, which comprises pre-incubating the sample prior to conducting the assay with an aqueous phase comprising a suspended phospholipid, wherein the phospholipid has a hexagonal (H_{II}) organization in aqueous detergent free media, wherein the aqueous phase comprises a detergent, wherein the phospholipid remains suspended in the aqueous phase for at least one hour at a temperature of about 25 deg. C. and wherein the phospholipid and detergent are [Sic, not] capable of interfering with the anticoagulant effect of heparin, anti-Factor antibodies and factor deficiencies.

61. A method of determining the presence of lupus anticoagulants in a patient's plasma which comprises the steps of:

(a) obtaining a first and a second sample of a patient's plasma;

(b) incubating the first sample with an aqueous suspension comprising a phosphatidylethanolamine;

(c) performing a lipid-dependent diagnostic assay on both the first and the second sample, the assay producing a positive reading when used on a sample which contains lupus anticoagulants; and

(d) comparing the results of the assays performed on the first and second samples, the presence of a normal result for the first sample and a positive result for the second sample being indicative of the presence of lupus anticoagulants in the plasma;

wherein:

the suspension of the phosphatidylethanolamine further comprises a lupus assay-compatible detergent;

the phosphatidylethanolamine remains in suspension at a temperature of 25ÅC for at least one hour;

the detergent, in combination with the phosphatidylethanolamine, is capable of inhibiting lupus anticoagulant, and not interfering with the anticoagulant effect of heparin, anti-Factor antibodies and factor deficiencies; and

the phosphatidylethanolamine is coated on a substrate bead, wherein the bead is composed of an inert material and wherein the bead has a diameter of from about 1 nm to 50 nm.

The prior art references relied upon by the examiner are:

Janoff et al. (Janoff)	4,698,299	Oct. 6, 1987
Huang	4,839,111	June 13, 1989

Madden et al. (Madden), AStabilization of Bilayer Structure for Unsaturated Phosphatidylethanolamines by Detergents,@ Biochemica et Biophysica Acta., Vol. 684, pp. 149-153 (1982)

BACKGROUND

The claimed invention relates to diagnostic assays, particularly for lupus anticoagulants, which employ phospholipid as assay reagents. Specification, page 1. The blood of patients with systemic lupus erythematosus (SLE) contains Alupus anticoagulants,@ Acoagulation inhibitors,@ or Alupus inhibitors@ which are believed to be antibodies against phospholipid which are produced by the immune system of patients suffering from SLE. Specification, page 2. Patients with diseases where anti-phospholipid antibodies are present are also likely to give false positive test results when subjected to lipid dependent diagnostic assays. Id.

The invention provides for a stable aqueous suspension of phospholipid particles for use in an assay for lupus anticoagulants. The phospholipid has a hexagonal organization when dispersed in an aqueous medium without detergent. Specification,

page 5, paragraph 2. The phospholipid remains in solution at a temperature of 25/C for at least one hour.

The claimed invention (claims 14 and 61) employs a lupus compatible detergent defined by appellants as 1) inhibiting lupus anticoagulant specifically; and
2) which does not interfere with the anticoagulation effects of heparin, anti-Factor antibodies, and factor deficiencies. Specification, page 5.

Grounds for Rejection

1. Claims 14-20 and 50-60 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden.

2. Claims 61-70 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden and Huang.

3. Claims 14-20 and 50-70 are rejected under 35 U.S.C. ' 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention.

35 U.S.C. ' 103

Claims 14-20 and 50-60 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden.

In rejecting claims under 35 U.S.C. ' 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion, or motivation to lead an inventor to combine those references. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629, (Fed. Cir. 1996) . Furthermore, the conclusion that the claimed subject matter is prima facie obvious must be supported by evidence, as shown by some objective teaching in the prior art or by knowledge generally available to one of ordinary skill in the art that would have led that individual to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

In the present case, the examiner relies on Janoff as evidence of lipid dependent diagnostic assays including pre-incubation of a plasma sample with a phospholipid in hexagonal organization. The preincubation step is shown to inhibit the activity of lupus anticoagulants which in turn reduces the number of false positives in coagulation tests. Answer, page 5. The examiner admits that the present claims differ from Janoff in that they

include a detergent to stabilize the phospholipid in the hexagonal organization. Answer, page 6.

To rectify this deficiency of Janoff, the examiner relies on Madden for establishing evidence of the use of detergents such as deoxycholate to stabilize the bilayer organization of phospholipid, increasing the temperature at which the bilayer to hexagonal transition occurs. Answer, page 6.

Thus, according to the examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to stabilize the phospholipid of Janoff with the detergent of Madden because Madden teaches that the use of detergents stabilizes phospholipid and to modify the assay of Janoff with a detergent as taught by Madden would have the expected result.

A prior art reference must be considered in its entirety, i.e. as a whole, including portions which would lead away from the claimed invention. W.L. Gore & Associates, Inc., v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). In the present case we find that the combination of references is without basis. Importantly, we find that Madden teaches away from the invention, as claimed.

The specification and Janoff ›299 both indicate that hexagonal lipids can reduce false positives in SLE assays, however, a lamellar or bilayer lipid structure Acompletely fails at this task.@ See Janoff ›299, column 4, line 63 to column 5, line 25; see also

specification page 4, lines 3-7 and Rauch page 9672, column 1.[2] Thus, one of ordinary skill in the art upon reading the disclosure of Janoff, would avoid the use of lamellar, i.e., bilayer, lipids in SLE assays.

Madden describes the stabilization of the bilayer structure for unsaturated phosphatidylethanolamines by detergents. In particular, Madden indicates that several common detergents, including sodium deoxycholate are able to stabilize the net bilayer organization for phosphatidylethanolamines under conditions where this structure is not available to either lipid species in isolation. Madden, page 149, column 2. Thus, Madden combines phosphatidylethanolamines with detergents such as deoxycholate, to achieve a stable lamellar bilayer structure. Janoff has described that such lamellar bilayer lipids give false positives in SLE assays and thus teaches to avoid their use. Therefore,

[2] Rauch et al (Rauch), AHuman Hybridoma Lupus Anticoagulants Distinguish between Lamellar and Hexagonal Phase Lipid Systems,@ Journal of Biological Chemistry, Vol. 261, No. 21, pages 9672-9677 (1986) was made of record in an Information Disclosure Statement filed April 30, 1992.

there would have been no motivation to one of ordinary skill in the art to use the stabilized lamellar bilayer structure achieved by Madden in the assay of Janoff, as Janoff teaches away from the use of such lamellar bilayer structures in SLE assays.

A reference may be said to teach away when a person of ordinary skill, upon examining the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1130, 1331 (Fed. Cir. 1994). In the present case, we find the combination of references to be without proper motivation, based on a teaching away from the combination of references as proposed by the examiner.

Moreover, Appellants argue that the claimed method requires a >lupus compatible detergent,=@ i.e., a detergent which is Aone which in combination with a selected phospholipid meets the following criteria: 1) inhibits lupus anticoagulant specifically; and 2) does not interfere with the anticoagulation effects of heparin, anti-Factor antibodies, and factor deficiencies.@ As indicated above, according to Janoff >299, lamellar bilayer structures such as that of Madden interfere with SLE antibodies, and thus would not qualify as a lupus compatible detergent as required by the claims.

In addition, the examiner has failed to particularly address the issues of particle

diameter, time and temperature as required by claims 14 and 50.[3] In view of the above, the examiner has not established a prima facie case obviousness and the rejection under 35 U.S.C. 103 over Janoff in view of Madden is reversed.

35 U.S.C. ' 103

Claims 61-70 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden and Huang.

[3] We find both the examiner=s and appellants' arguments with respect to the teachings of the particle size of the lipid particles of Madden to be confusing, especially in view of the fact that an inaccurate conversion of Angstroms to nanometers (nm) has been made and relied upon in the record. We note that the 1000 D diameter phospholipid of Madden (page 150, column 2) converts to 100 nm and not 10,000 nm as argued by appellants and as accepted by the examiner. Brief, page 4; Answer, page 9.

The combination of Janoff and Madden is discussed above. Huang is relied on by the examiner for the disclosure of solid core colloidal gold particles coated with phospholipid derivatives. The solid core liposomes of Huang comprise bilamellar lipid particles. See abstract. In contrast, the coated beads as depicted in Figure 2 of the present invention comprise a bonding layer over which is applied a phospholipid monolayer. Specification, page 12, paragraph 1. It would appear that the coated gold particles of Huang and the claimed particles are of a different lipid structure.

We find that Huang fails to overcome the above noted deficiencies of the combination of Janoff and Madden. Therefore, the rejection of claims 61-70 over Janoff in view of Madden and Huang is reversed.

35 U.S.C. ' 112, second paragraph

Claims 14-20 and 50-70 are rejected under 35 U.S.C. ' 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention. The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. ' 112, second paragraph, is whether the claims meet the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. As stated above, if the scope of a claim would be reasonably ascertainable by those skilled in the art, then the

claim is not indefinite. See Ex parte Porter, 25 USPQ2d 1144, 1146 (Bd. Pat. App. & Int. 1992).

The examiner argues that the terms Athe presence@, Apositive reading@, Apositive result@, Anormal result@ are not understood and it is not clear what is intended by these claim terms. Answer, page 8. The examiner also argues Athe test sample employed@ lacks antecedent basis in claim 15, and the term Athe concentration lacks antecedent basis in claim 18. We find the scope of the above claim terms would be reasonably ascertainable by those skilled in the art since a person of skill in the art would understand operation of the invention from the specification in view of the level of knowledge described. Ex parte Porter, 25 USPQ2d 1144, 1146 (Bd. Pat. App & Int. 1992); In re Goffe, 526 F.2d 1393, 188 USPQ 131 (CCPA 1975); In re Moore, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971); In re Hammack, 427 F.2d 1378, 166 USPQ 204 (CCPA 1970). In view of the above, the rejection of Claims 14-20 and 50-70 are rejected under 35 U.S.C. ' 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention is reversed.

Other Matters

The examiner has noted (Answer, page 9) and Appellants have recognized (Brief, page 3) that the recitation in claim

50 that the phospholipid and detergent Ais capable of interfering with the anticoagulant effect of heparin, anti-Factor antibodies, and factor deficiencies,@ is incorrect. The claim should read that the phospholipid and detergent are not capable of interfering with the anticoagulant effect of heparin, anti-Factor antibodies, and factor deficiencies. Upon return of the application to the examiner, rectification of this error should be made.

We note the appellants have submitted an incomplete copy of the claims in the Brief, and the Examiner has not provided a clean copy of the claims for our review (claim 70). In addition, we note the Information Disclosure Statement filed April 30, 1992 has not been properly acknowledged by the examiner. Although an additional and overlapping Information Disclosure Statement was filed August 1, 1994, they did not completely overlap and thus some of the earlier filed references were not properly acknowledged by the examiner. Upon return of the application to the examiner, proper processing of the Information Disclosure Statement of April 30, 1992 is encouraged.

CONCLUSION

The rejection of Claims 14-20 and 50-60 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden is reversed. The rejection of Claims 61-70 are rejected under 35 U.S.C. ' 103 as unpatentable for obviousness over Janoff in view of Madden and Huang is reversed. The rejection of Claims 14-20 and 50-

70 are rejected under 35 U.S.C. ' 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention is reversed.

REVERSED

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR ' 1.136(a).

Carol A. Spiegel Administrative Patent Judge	)
Toni R. Scheiner Administrative Patent Judge	) BOARD OF PATENT)) APPEALS AND)) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

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